

The Treatment of Acute Hematogenous Osteomyelitis with Penicillin and Sulfonamides Combined*

SAMUEL S. MATHEWS, M.D., and CHARLES G. HUTTER, JR., M.D., *Los Angeles*†

THE prognosis in acute hematogenous osteomyelitis is changing for the better in respect to mortality rate, complications, and the degree of disability produced by the bone lesions. The addition of chemotherapy and penicillin to the treatment of the disease is mainly responsible for this marked improvement in its outcome. Since it is oftentimes difficult to appreciate the beneficial effects which new treatments obtain unless careful comparisons are made with the course of patients treated by previous methods, an analysis was made of the records of all cases of acute osteomyelitis due to the staphylococcus which were admitted to the Los Angeles Children's Hospital in the years from 1941 to 1946. The cases were divided into two groups, according to the type of treatment they received.

From 1941 to 1944 there were 16 admissions for acute osteomyelitis. During the acute stage of the disease this group of patients received the derivations of sulfanilamide in one form or another, usually sulfadiazine. During 1944 and 1945 there were nine admissions. These were treated with a combination of penicillin and one of the sulfonamides, and for clarity this group will be referred to throughout this article as the penicillin treated group.

Osteomyelitis is a relatively uncommon disease and this is an insufficient number of cases to establish a statistically valid series but an analysis of these case records nevertheless brings to light certain trends which indicate a more satisfactory prognosis for this disease under its present management.

The mortality in our series of cases was zero. This trend agrees with the conclusions of Kenney⁶ who made an extensive study of the mortality rate of osteomyelitis before and since the introduction of chemotherapy. He arrived at the mortality rates from a comparative study of 3,000 cases of acute osteomyelitis which had been reported in the medical literature.

He found that the change from immediate surgical drainage to one of delayed surgical intervention in the acute cases, as adopted about 1934, resulted in a fall in the mortality rate from around 40 per cent to a new low of 23 per cent. Chemotherapy was then introduced and its use succeeded in lowering this figure still further to about 3 per cent. More recently the addition of antibiotics to chemotherapy has reduced the mortality rate to a still lower figure, for penicillin is much more effective than sulfadiazine

in sterilizing the staphylococcus infected blood stream. Altemeier and Helmsworth¹ reported a series of 34 cases which they treated with penicillin without mortality and several other authors have reported a smaller series with essentially the same mortality figures. With the extensive use of penicillin early in the treatment of these staphylococcus infections we feel that we can anticipate a reduction of the mortality rate to less than 1 per cent.

The addition of penicillin did not appreciably reduce the number of days of hospitalization of our series. The average number of days of hospitalization of the group treated with the sulfonamides was 51, while the average for the cases treated with a combination was 47 days. (Figure 1.)

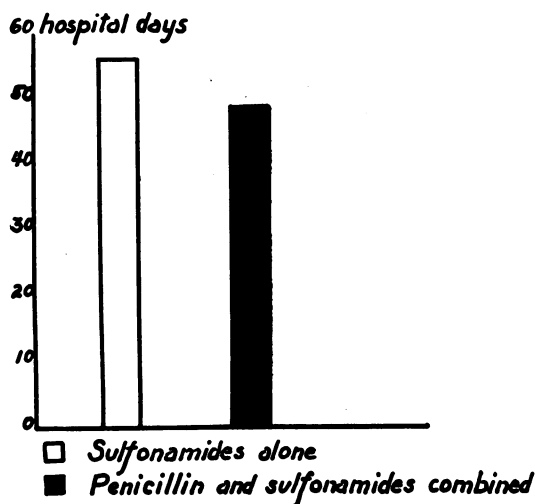


Figure 1.—Diagrammatic representation of the average number of hospital days in 25 cases of staphylococcus osteomyelitis.

To compare the course of the disease as reflected by the elevations in temperature we made a composite chart of the average daily high and low temperature of these patients during their first two weeks of hospitalization. It reveals a considerable difference in the course of the disease in the patient treated with penicillin as compared with that in the patient treated with sulfadiazine. Both groups started out with approximately the same temperature level but while the fever of the group treated with the sulfonamides alone continued to fluctuate daily for the first week to about 101 degrees, that of the penicillin-treated group usually fell to a 99 degree level at the end of the third day. This striking difference between penicillin-sulfa therapy and sulfonamide

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† M. J. Connell Research Foundation, Children's Hospital, Los Angeles.

treatment in influencing the duration of clinical signs of infection is best visualized on the accompanying diagram. It must be remembered that this composite temperature chart does not reflect the considerably greater individual variations in their response to the disease process. (Figure 2.)

Anderson *et al.*,³ Altemeier and Helmsworth¹ and others in studying cases reached this same conclusion regarding an effective shortening which penicillin produces in the number of days of elevated temperature.

Studies have been made of the effect of penicillin on the bone lesions as visualized by repeating x-ray films of the affected part. Altemeier and Reinecke² found that a few of their cases with clinical signs of osteomyelitis and positive blood cultures did not show any bony changes. They believed they were justified in dividing their patients into two groups. In one group they felt penicillin therapy had been started early enough in the course of the disease to sterilize the blood stream before bone abscess and destruction took place, while in the other group the treatment had been delayed several days and it was their belief that this delay resulted in secondary changes observable in the roentgenograms of the bone involved. They suggest that the degree of bone destruction as visualized on the x-ray film depends upon how long the treatment has been postponed.

In our series we did not find this to be true. All of our cases eventually showed bone changes which were discernible by x-ray, even one case in which we believe penicillin was started on the first day of appearance of clinical signs of the infection. In the absence of bone changes which can be visualized on x-ray film it is difficult to judge whether the patient has osteomyelitis or merely a staphylococcal septi-

cemia. In our cases bone changes are a requisite for the diagnosis of osteomyelitis. In the cases exhibiting more severe bone changes, rarefaction and absorption of the calcium salts continued for the first two to three months after the acute infection. This change was unaccompanied by any systemic evidence of infection, however, suggesting that it was not the result of a chronic bone infection but rather the continued absorption of bone damaged during the acute stage of the infection. After this variable period of time the x-rays reveal areas of decreased density and bone replacement, suggesting a healing of the bone.

It is difficult to compare the x-ray changes in cases treated by the penicillin-sulfa combination with those in cases treated with sulfadiazine. It can only be stated that on comparing them one gains the definite impression that the combination prevents severe bone lesions.

With this accumulating evidence indicating that penicillin has lessened the degree of bone damage and abscess formation, the question of the optimum time and necessity for surgical drainage is again raised. From a review of the literature on the problem one concludes that non-surgical intervention in the treatment of the bone lesion is becoming more desirable when the patient is under penicillin therapy. In the review of our series one of the most striking features is the sharp drop in the incidence of surgical intervention in the penicillin-treated group. In the group treated with the sulfonamides, 90 per cent had surgical intervention, with incision and drainage, or else decortication in one form or another and packing with vaseline gauze. In contrast, only 20 per cent of the penicillin-treated group had surgical drainage, and then only aspiration of the soft tissue accumula-

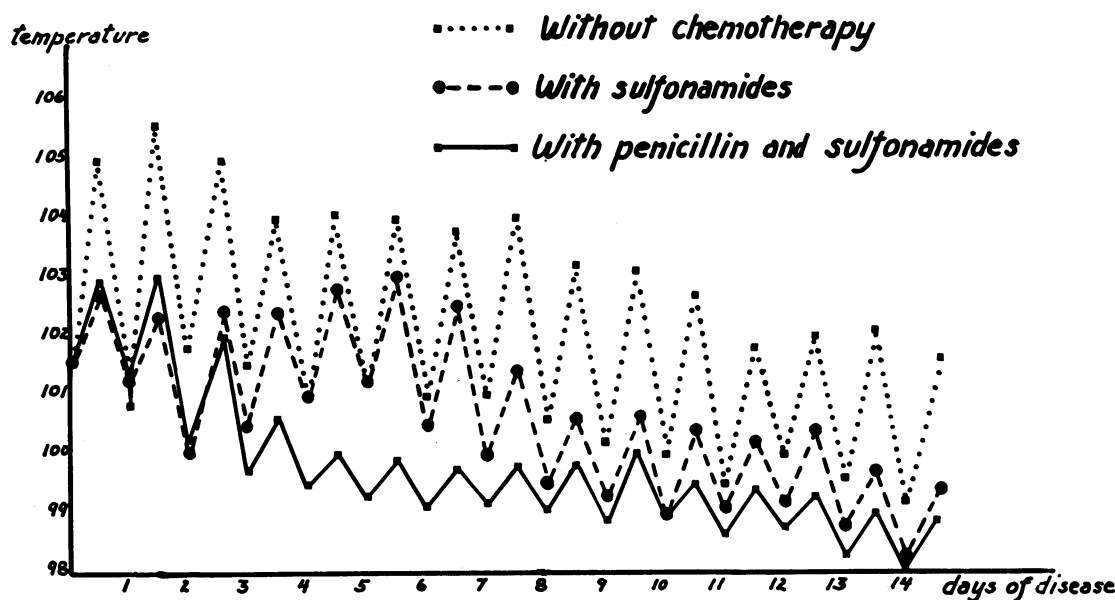


Figure 2.—Composite chart of the average daily high and low temperatures of osteomyelitis cases under different forms of therapy.

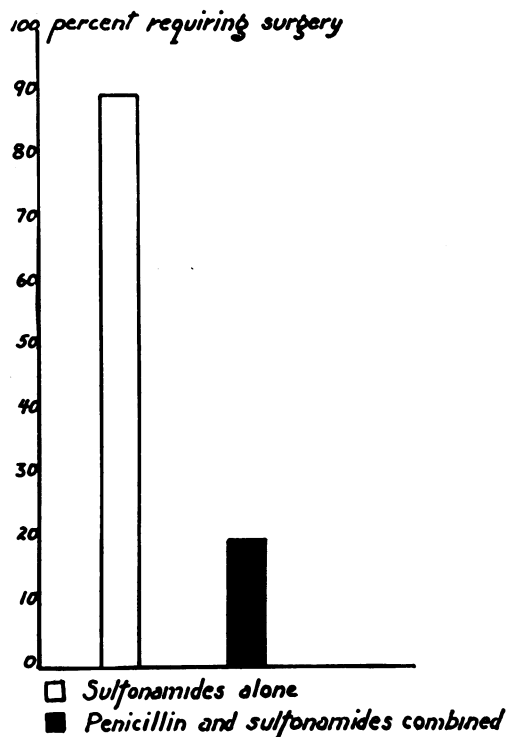


Figure 3.—Chart comparing the percentage of cases which had surgical drainage before and since the addition of penicillin to sulfonamide treatment of osteomyelitis.

tions of purulent material. A small incision for drainage of a soft tissue abscess was carried out in two cases. (Figure 3.)

A Stanford University group under Bloomfield⁴ believes that adequate early arrest of the disease with penicillin will do away with surgery entirely.

Dickson⁵ is perhaps the strongest supporter of early surgical drainage. He feels that one should produce an avenue of escape for entrapped purulent material in all bone abscesses where there is no evidence of continuing systemic infection and where there is definite evidence by x-ray of bone localization. Our series certainly indicates that with penicillin therapy few need surgery and we hesitate to institute any procedures which might introduce secondary infection until such become absolutely necessary. It has been our experience in treating these cases and deciding upon surgical intervention that several other important factors must be borne in mind.

The first of these in importance is the type of infection from which the patient suffers. Is it a septicemia with the bony lesion playing only a small part in the generalized process, or is it a localizing bone abscess following a transient bacteremia? In a certain number of the cases the infection is a generalized one with multiplication of the organism in the blood stream and secondary abscess formation in the bony, hepatic, pulmonary or other systems. Is it not unwise to operate and drain in such cases?

A greater number of cases of osteomyelitis have a transient bacteremia, with the development of a

bone abscess during the first few days of the infection. Drainage of such an abscess, after the body has been able to control the initial stages of infection, may prevent its further subcortical spread and involvement of the shaft and thereby shorten the period of disability and destruction of the disease. X-ray changes showing increased density do not necessarily mean purulent accumulation. Soft tissue fluctuation is a better indication for drainage. The procedure might be incision of the soft tissues and decortication over the most destroyed area, suturing into the wound a catheter to maintain drainage and facilitate the instillation of penicillin locally each day, with closure of the incision by stainless steel retention sutures to prevent secondary infection.

Many fluctuant subcutaneous abscesses can be drained easily by aspiration, for with penicillin therapy the pus tends to be thin, rather than thick and filled with necrotic debris as is generally characteristic of staphylococcal infections. Should this procedure not suffice, further surgical measures can then be instituted.

Any comparison between the recurrences of infection and subsequent metastatic complications in these two groups must be postponed until there has been a considerable passage of time.

TREATMENT

If we expect to reduce the mortality rate in acute hematogenous osteomyelitis to less than 1 per cent and to keep the bone destruction at an absolute minimum adequate early treatment of the disease is essential. The following outline covers the major features of such treatment.

1. Complete examination with x-rays of the affected parts, plus a chest film.
2. A hemoglobin, red blood count, white blood count, and differential count on admission with the hemoglobin, white blood count and differential repeated every other day for the first week or for the duration of the acute stage, then once weekly.
3. Urine examination on admission and every other day during the acute stage, then bi-weekly.
4. Blood culture on admission and every other day until three cultures are negative.
5. Donors secured and blood matched. 150 to 200 cc. daily if indicated; at least once a week, depending on the hemoglobin level.
6. Penicillin, intravenous route if necessary, 400,000 units or more daily for the first day or two, then somewhat smaller dosage until the patient is well.
7. Sulfadiazine in adequate amounts to maintain a blood level of about 12 mgm. per 100 cc. of blood. A high dosage may be necessary to secure this blood level.
8. Positive fluid balance with adequate output of urine by use of intravenous fluids if necessary.
9. Immobilization of affected parts with splints, plaster, or traction, taking care to avoid injuring the skin with adhesive.
10. High vitamin diet with accessory vitamins by mouth or intravenously.

SUMMARY

A comparative study of the effectiveness of the sulfonamides alone and of the sulfonamides and penicillin combined in the treatment of 25 cases of hematogenous staphylococcus aureus osteomyelitis at the Children's Hospital, Los Angeles, is presented. It shows the expected mortality rate of penicillin treated cases of osteomyelitis should be less than 1 per cent; that the course of the disease as reflected by the temperature charts is considerably shortened; that the roentgenograms reveal less destruction in these cases and that the necessity for surgical intervention and drainage of bone abscesses has been markedly reduced.

An outline of the essentials for the adequate treatment of acute osteomyelitis is presented.

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Quinidine in Heart Disease, Particularly in the Older Age Groups*

S. A. WEISMAN,† M.D., *Los Angeles*

THE value of quinidine in the treatment of the acute cardiac arrhythmias seems to be well accepted. However, reports frequently appear in the literature emphasizing that it should be used only in the acute arrhythmias in young persons with no underlying heart disease and warning against its use in (1) patients in the older age group, (2) auricular fibrillation of more than three months' duration, (3) coronary sclerosis with fibrillation, (4) heart failure with fibrillation and (5) coronary thrombosis. Quinidine thus would be contraindicated in groups representing perhaps the majority of all cardiac arrhythmias.

The average age of the population in the United States is increasing. The latest statistical report shows that more than one half of our population is over 30 years of age.¹⁶ On the Pacific coast the average age is higher than in any other section of this country.¹⁵ The median age of residents is higher in California than in any other state. At 33 years it is more than three years higher than the median age for the nation as a whole. The life expectancy at birth among the policy holders of the Metropolitan Life Insurance Co. in 1945 is 65 years, 14 years higher than it was just 25 years ago. In the United States today, cardiac disease is the chief cause of death. A number of studies are being conducted on the causes and the prevention of various cardiac diseases. It is hoped that rapid progress in this field will be made. However, for the present we must be prepared to treat a constantly aging population affected with increasing

numbers of cardiac disorders. That the medical profession is cognizant of this fact is evidenced by the recent appearance of a medical periodical restricted to geriatrics.

In our experience of many years we have found the greatest value of quinidine to be in the older age group. In our first clinical report,²² 80 per cent of our successfully treated cases of auricular fibrillation were in patients 50 years of age or older. Since 1929 we have treated more than 500 cases of auricular fibrillation with a successful restoration to normal rhythm in about 70 per cent of cases. Of this percentage by far the greater part comprises cases in the older age group. Many of these patients were cardiac invalids materially benefited by the restoration to normal cardiac rhythm. Two of them had been successfully carrying on in their daily duties for ten years when last seen in 1942.

In most instances effort should be made to restore an irregular beating heart to normal rhythm. The cardiac output of a fibrillating heart is 15 to 79 per cent less than it is when the heart has been restored to normal rhythm.^{3,11} Clinical and experimental studies show that the average difference is 20 to 30 per cent.^{7,14} This is a considerable variation in cardiac efficiency. An irregular heart causes a slowing of the circulation and an increase in venous pressure. This leads to an overfilling of the heart. Thus a vicious circle is established.⁶

CASE REPORTS

CASE 1: A farmer, aged 72 years, had been reporting to the clinic for more than two months. His chief complaint was marked dyspnea, weakness, and swelling of the ankles and legs. He had been digitalized. The heart rate was 70 but the beat was irregular. Congestion rales were present in the bases

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†From the Department of Medicine, University of Southern California, and the Department of Medicine, Los Angeles County Hospital, Los Angeles.